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Effect of Surfaces on the Aggregation of Hydrophobic and Hydrophilic Amyloidogenic Peptides

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The general effect of surface hydrophobicity/hydrophilicity on the aggregation of peptides is studied by simulations of oversaturated aqueous solutions of hydrophobic and hydrophilic peptides in pores with hydrophobic (paraffin-like) and hydrophilic (silica-like) walls. Strong adsorption of peptides on the pore walls is observed in the case of the hydrophobic peptides in a hydrophobic pore, where all peptides are strongly adsorbed and aligned parallel to the walls already after 30 ns. Adsorption of this peptide at the liquid-vapor interface is quite similar. In the other three cases considered, the peptides are repelled from the walls, localized near the pore center and do not show orientational ordering with respect to the walls. Our results show that even a single factor such as the water density distribution has a drastic effect on the character of peptide aggregation near surfaces. A wider diversity of possible scenarios can be expected when specific peptide-surface interactions are taken into account.

Adsorption of peptides on surfaces can strongly affect their aggregation. Possible enhancement of the orientational ordering of peptides near surfaces can promote the formation of ordered peptide aggregates. This may be one of the factor, which makes the intracellular and extracellular aggregation different. To explore the general effect of surface hydrophobicity/hydrophilicity on peptide adsorption and aggregation, we performed a series of computer simulation studies on oversaturated aqueous solutions of peptides in slit-like pores with smooth walls interacting via a (9-3) LJ potential with water molecules and non-interacting with peptides. Two kinds of amyloidogenic peptides were used: the hydrophobic peptide NFGAIL, (residues 22-27 of the human islet amyloid polypeptide), and the polar hydrophilic peptide GNNQQNY (residues 7-13 of the yeast prion Sup35).

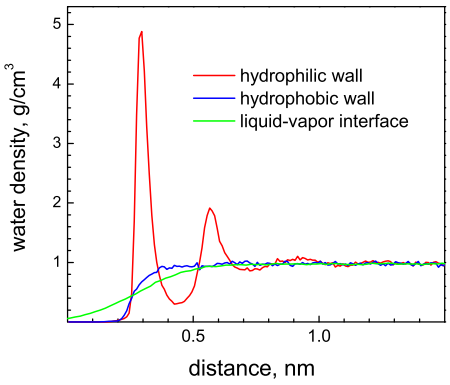

Figure 1. Water density profiles near hydrophobic and hydrophilic walls and at the liquid-vapor interface.

Two kinds of pore walls were considered: a hydrophobic paraffin-like wall, which causes a pronounced water density depletion near the surface (see the blue line in Fig. 1), and a hydrophilic silica-like wall, which causes formation of two highly ordered water layers near the surface (see the red line in Fig. 1). Additionally, we have simulated a liquid-vapor interface of the aqueous solution of hydrophobic peptides (its density profile is shown by the green line in Fig. 1).

Six peptide fragments were randomly inserted in a cubic box of length 6 nm such that the peptides are at least 0.7 nm away from each other and 0.15 nm away from the surfaces. All atomic molecular dynamic simulations were carried out at T = 330 K with Gromacs software using the OPLS force field and SPCE water molecules.[1] The PME method was used to treat long range electrostatic interactions.[2] Five simulations with different initial velocities were carried out for the duration of 70 ns for each type of surface and peptide combination.

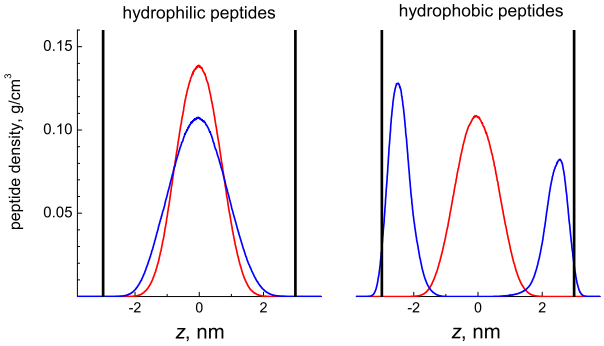

Figure 2. Density profiles of hydrophilic (left) and hydrophobic (right) peptides in the pores with hydrophilic (red) and hydrophobic (blue) walls. Vertical black lines indicate locations of the pore walls. The pore center is located at z = 0.

The density profiles of the peptide in pores, calculated by taking into account all peptide atoms, are shown in Fig. 2. Hydrophilic peptides show strong desorption from both hydrophilic and hydrophobic surfaces and concentrate near the pore center (see left panel in Fig. 2). The repulsion of these peptides is slightly stronger in the case of a hydrophilic surface. Hydrophobic peptides exibits a quite similar desorption characteristics from a hydrophilic surface (see red line in the right panel in Fig. 2). An opposite behavior is observed for the hydrophobic peptides in hydrophobic pore: in all simulation runs, the peptides are strongly adsorbed at the walls already after 20 to 30 ns (see blue line in the right panel in Fig. 2). As the peptides do not interact with the pore walls, the tail of peptide's density profile crosses the pore wall. Quite similarly, hydrophobic peptides strongly adsorb at the liquid-vapor interface (not shown), which also has a strong hydrophobic character.

A strong adsorption of the peptides at the surface enhances their orientational ordering. The probability distribution of the angle α between the pore surface and the vector connecting two most distant peptide heavy atoms is shown in Fig. 3. When peptides are repelled from the pore walls and localized in its center, the orientation of their longest axis is highly isotropic (left panel in Fig. 3). In contrast, strong adsorption of the peptides at

the surface causes their longest axis aligned parallel to the walls. Thus, adsorption at the surface not only speeds up their aggregation, but also provides favourable conditions for the formation of ordered peptide aggregate characterized by extensive β-sheet formation.

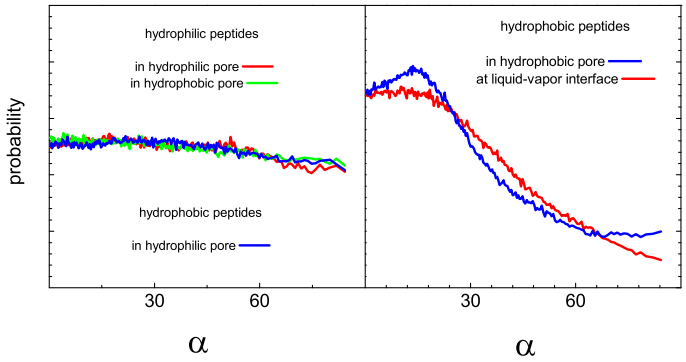

Figure 3. Probability distribution of the angle α between the pore surface and the vector connecting two most distant peptide heavy atoms.

The results shown in Figs. 2 and 3 evidence that even a single factor such as the water density distribution near a surface has a drastic influence on the peptide aggregation. Hence, the surface effects are expected to be much more important in the case of intracellular peptide aggregation. Presumably, such surface effects and the effect of the finite size of biological cells[3] are the two main factors rendering the intracellular and extracellular peptide aggregation processes different.

Acknowledgments

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